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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/930,832
Filing Date	August 15, 2001
First Named Inventor	KAY, MARK A.
Group Art Unit	1648
Examiner Name	WINKLER, ULRIKE
Attorney Docket Number	STAN-107DIV
Total Number of Pages in This Submission	5

ENCLOSURES (check all that apply)

- [ ] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment / Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
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- [ ] Information Disclosure Statement
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- [ ] Proprietary Information
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- [x] Other Enclosure(s) *(please identify below)*:

Petition for Certificate of Correction;
Certificate of Correction;
Marked up copy of Column 1 of specification;
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Signing Attorney/Agent (Reg. No.)	**BRET E. FIELD, 37,620** **BOZICEVIC, FIELD & FRANCIS, LLP**
Signature	
Date	SEPTEMBER 8, 2006

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PETITION FOR CERTIFICATE OF CORRECTION Address to: Mail Stop DAC Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Attorney Docket	STAN-107DIV
	First Named	KAY, MARK A.
	Patent Number	7,045,344
	Issue Date	May 16, 2006
	Application	09/930,832
	Filing Date	August 15, 2001
	Title: *"NOVEL ADENOVIRAL VECTOR AND METHODS FOR MAKING AND USING THE SAME"*	

Sir:

Transmitted herewith for filing is a Certificate of Correction for the above-identified patent.

Please enter the correct Grant No in:

Column 1, in the specification under ACKNOWLEDGMENT, second line should read --support under Grant No. NIH **DK** 49022 awarded by --

The Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. § 1.20, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815 order number STAN-107DIV.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

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(Also form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 7,045,344

DATED : May 16, 2006

INVENTOR(S) : KAY, MARK A., et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 1, In the specification under ACKNOWLEDGMENT, second line should read
--support under Grant No. NIH **DK** 49022 awarded by --

MAILING ADDRESS OF SENDER:

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PATENT NO. 7,045,344

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ADENOVIRAL VECTOR AND METHODS FOR MAKING AND USING THE SAME

CROSS REFERENCE TO RELATED APPLICATIONS

Pursuant to 35 U.S.C. § 119 (e), this application is a divisional of U.S. patent application Ser. No. 09/428,292, filed Oct. 27, 1999 now U.S. Pat. No. 6,303,362 which claims priority to the filing date of the United States Provisional Patent Application Ser. No. 60/109,057 filed Nov. 19, 1998, the disclosure of which is herein incorporated by reference.

ACKNOWLEDGMENT

This invention was made with United States Government support under Grant No. NIH DK 49022 awarded by National Institutes of Health. The United States Government has certain rights in this invention.

INTRODUCTION

1. Field of the Invention

The field of this invention is nucleic acid vectors, particularly adenoviral based vectors.

2. Background of the Invention

The introduction of an exogenous nucleic acid sequence (e.g. DNA) into a cell, a process known as "transformation," plays a major role in a variety of biotechnology and related applications, including research, synthetic and therapeutic applications. Research applications in which transformation plays a critical role include the production of transgenic cells and animals. Synthetic applications in which transformation plays a critical role include the production of peptides and proteins. Therapeutic applications in which transformation plays a key role include gene therapy applications. Because of the prevalent role transformation plays in the above and other applications, a variety of different transformation protocols have been developed.

In many transformation applications, it is desirable to introduce the exogenous DNA in a manner such that it is incorporated into a target cell's genome. One means of providing for genome integration is to employ a vector that is capable of homologous recombination. Techniques that rely on homologous recombination can be disadvantageous in that the necessary homologies may not always exist; the recombination events may be slow, etc. As such, homologous recombination based protocols are not entirely satisfactory.

Accordingly, alternative viral based transformation protocols have been developed, in which a viral vector is employed to introduce exogenous DNA into a cell and then subsequently integrate the introduced DNA into the target cell's genome. Viral based vectors finding use include retroviral vectors, e.g. Maloney murine leukemia viral based vectors. Other viral based vectors that find use include, HSV derived vectors, sindbis derived vectors, etc. One type of viral vector of particular interest is the adenovirus derived vector.

Recombinant adenovirus vectors have been shown to have great promise for the gene transfer in basic research as well as clinical treatment of many diseases. They can transduce foreign genes efficiently into both cultured cells and many target organs in vivo. There are more forty different serotypes of adenovirus (Ad) identified. The Ad type 5 genome has been most commonly used to make recombinant Ad vector. The genome of human Ad is a linear 36 kb, double-stranded DNA genome that encodes more than 50 gene products. In the first generation Ad vector, the early region 1 (E1) is replaced by the foreign gene and the virus propagated in an E1-transcomplementing cell line such as 293. By deleting E1 and early region 3 (E3) sequences up to about 8 kb of foreign gene can be inserted. However, in vitro manipulation of Ad DNA is difficult. Unique and useful restriction sites are limited because of the large size of the genome, making the construction of Ad vector relatively labor intensive. Two standard methods to make E1-deleted Ad vector have been developed: an in vitro ligation method and a homologous recombination method in 293 cells.

The in vitro ligation method uses whole viral DNA genomes and the plasmid containing the left end of Ad with the right inverted terminal repeat (ITR), the packaging signal and E1A enhancer sequence (map unit; 0 to 1.3). After the gene of interest is inserted into the downstream of the viral sequence of the plasmid, the fragment containing viral sequence and gene of interest is excised and ligated to the unique ClaI site (map unit; 2.6), replacing a portion of the viral E1 region. Then, the ligated DNA is directly transfected into 293 cells to make recombinant virus. However, this method is rarely used today because the efficiency is low and the recombinant virus requires purification of contaminating wild type and transgene null viruses related to incomplete restriction digestion and self-religation.

One system using homologous recombination uses two plasmids with overlapping fragments that recombine in vivo. The first plasmid contains the entire Ad genome with a deletion of the DNA packaging and E1 region. The second plasmid contains right ITR, packaging signal and overlapping sequence with the first plasmid. After the gene of interest is introduced into the second plasmid, the two plasmids are co-transfected into 293 cells. The virus, which is produced by the recombination in 293 cells, is isolated through plaque purification. The major limitation to this approach is that the recombination event occurs at a low frequency.

Newer methods for adenoviral preparation are based on homologous recombination of two plasmids using yeast artificial chromosomes or bacteria. These methods, while more efficient, are more complex. The YAC system requires yeast culture and manipulation while the *E.coli* system requires three step transformations using an additional non-conventional host bacterial strain (BJ5183recBCsbcBC).

Accordingly, there is continued interest in the development of new methods for preparing recombinant adenoviral vectors. Of particular interest would be the development of a method which is highly efficient and yet requires a minimum number of steps.

Relevant Literature

of interest include: U.S. Pat. Nos. 5,962,313; 5,962,311; 5,952,221; 5,932,210; 5,928,944; 5,922,576; 5,919,676; 5,891,690; 5,885,808; 5,880,102; 5,877,011; 5,871,982; 5,869,037; 5,858,351; 5,851,806; 5,843,742; 5,837,484; 5,820,868; 5,789,390; 5,756,283; 5,747,072; 5,731,172; 5,700,470; 5,670,488; 5,616,326; 5,589,377; 5,585,362; and 5,354,678.

Other references of interest include: Berkner, et al., (1983). Generation of adenovirus by transfection of plasmids. Nucleic Acids Res. 11, 6003–6020; Bett, et al. (1994). An efficient and flexible system for construction of adenovirus vectors with insertions or deletions in early regions 1 and 3. Proc Natl Acad Sci USA. 91, 8802–6; Chartier, et al. (1996). Efficient generation of recombinant adenovirus vec-